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OM protein - protein search, using sw model

Run on: May 7, 2002, 12:00:48; Search time 53.91 Seconds

(without alignments)
195.111 Million cell updates/sec
742
Sequence: 1 MAVIVLELCLVAFFSCVLSQ......MKRGYAMDYWGQGTLVTVSS 142
Scoring table: Gapop 10.0, Gapext 0.5
Searched: 522463 seqs, 74073290 residues
al number of hits satisfying chosen parameters: 522463
Minimum DB seq length: 0
Maximum Match 08
Maximum Match 08
Maximum Match 1008
Listing first 45 summaries
```

A_Geneseq_1101:*

| SIDSB/gcgdata/geneseq/geneseqp/AA1980.DAT:*
| SIDSB/gcgdata/geneseq/geneseqp/AA1981.DAT:*
| SIDSB/gcgdata/geneseq/geneseqp/AA1991.DAT:*
| SI

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

Description Humanised anti-CTL Mouse antibody 26 Heavy chain of Hum Murine anti-human Ganglioside GD2 sp Humanised anti-CD3 Sequence of the he Heavy chain of Mum MAD 10.1 heavy cha NEWM humanised 2B6 Murine mik-betal a
Ouery Ouery Autch Length DB ID Aug 89.5 142 22 AAG6523 664 89.5 142 22 AAG6520 3.5 81.3 137 18 AAW30273 654 73.5 140 18 AAW30273 657 71.4 151 17 AAR9841 7.5 71.1 137 18 AAW3027 7.5 71.0 138 17 AAW9145 7.5 70.8 119 17 AAR9492 7.5 70.8 119 17 AAR9492
Length 1 142 142 137 137 151 151 135 138 138
% Ouery Match 100.0 89.5 81.3 73.5 73.0 71.4 71.1 71.0 71.0 71.0 71.0 71.0 71.0 71.0
Score 742 664 603.5 541.5 530 527.5 527.5 527.5
Result No. 12 2 2 2 3 3 4 4 4 4 4 7 7 10 10 11 11

	vy chain var 2 chimeric a i-IL2R-alpha	avy cl n var antil	VII (LK)-VI Of anti Anti-idiotype mono TM27 antibody VH c	Humanised anti-CD3 Ganglioside GD2 sp	antibody VE lioside GD2 antibody VH	Intibody VH YPe murine Intibody VH	able heavy ch 3 heavy chai	murin murin murin	TO 22 11 11 77
9 19 AAW4247 8 18 AAW0894 5 17 AAW0582 8 17 AAW0582 17 AAW0582 18 AAW0582	12 AAR15	20 AAY2846 20 AAY2154 20 AAY2154 20 AAY2847	17 AAW0320 20 AAY2243 17 AAB0804	22 AAB8197 20 AAY2243	22 AAB8197 20 AAY2243	70 10 10 10 10 10 10 10 10 10 10 10 10 10	15 AAR5333 20 AAY2835	18 AAW1054 18 AAW0743	
22 70.4 119 18 69.8 138 5 69.5 116 5 69.5 273 5 69.5 448 15 69.4 138	69.4 69.4	699.3	68.6 68.4 1	5 68.0 1	5 68.0 5 5 67.9 1 5 67.7 1	67.2	66.4	4 # # #	65.5 65.4 111 65.4 112 65.3 113
12 52; 13 518 14 515; 15 515; 16 515; 17 515;		ហហហ	507	504	504 503 502	498. 497.	492. 492. 491.	488. 486.	485. 485. 484.

ALIGNMENTS

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Human; CTLA4; cytotoxic T lymphocyte associated antigen 4; anti-CTLA4;
immunosuppressive; immunomodulator; antiallergic; vaccine; antibody;
T cell; humanised antibody; autoimmune disorder; graft rejection;
allergy; heavy chain.
                                                                                                                                                                                                                                                                                                 Carreno BM, Wood C, Turner K, Collins M, Gray GS, Morris D; O'Hara D, Hinton P, Tsurushita N;
                   AAG66523 standard; Protein; 142 AA.
                                                                              Humanised anti-CTLA4 heavy chain.
                                                                                                                                                                                                                                    26-JAN-2001; 2001WO-US02653.
                                                                                                                                                                                                                                                        27-JAN-2000; 2000US-0178473.
                                                             (first entry)
                                                                                                                                                                                                                                                                                                                               WPI; 2001-483195/52.
N-PSDB; AAH76441, AAH76443.
                                                                                                                                                                                                                                                                             (GEMY ) GENETICS INST INC.
                                                                                                                                                                                            WO200154732-A1.
                                                                                                                                                     Homo sapiens.
                                                                                                                                                                  Mus musculus.
                                                          22-OCT-2001
                                                                                                                                                                                                                 02-AUG-2001.
                                                                                                                                                                            Synthetic.
                                       AAG66523;
           AAG66523
RESULT
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Best Local Sim
Matches 142;
                                                                                  AAG66520;
                                          Sequence
                                               Query Match
                                       antibody
      response
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The invention relates to an antibody-toxic group conjugate comprising on antibody that specifically recognises a molecule expressed only on a cativated T cells, and a toxic group. The T cell molecule is CC artivated T cells, and a toxic group. The T cell molecule is CC preferably human cytotoxic T lymphocyte associated antigon 4 (CTLA4). CC comprising a sequence of 128 or 142 amino acids fully defined in the comprising a sequence of 128 or 142 amino acids fully defined in the CC specification. The antibody-toxic group conjugate is useful for a condulating the immune response to a manune response to a graft, or condition such as autoimmune disorder, immune response to a graft, or allergic response or an immune response to a therapeutic protein.

T callergic response or an immune response to a therapeutic protein.

T callergic response or an immune response to a graft, or and isolating CTLA4-bearing cells. The antibody is also useful for research purposes, e.g., in staining fragments of the receptor, for vaccine preparation, and for determining fragments of the receptor, for vaccine preparation, and for determining free effectiveness of an agent to down-regulate CTLA4 activity. The preparation sequence is the heavy chain of humanised anti-CTLA4 . 0 Mouse: CTLA4; cytotoxic T lymphocyte associated antigen 4; anti-CTLA4; immunosuppressive; immunomodulator; antiallergic; vaccine; antibody; T cell; humanised antibody; autoimmune disorder; graft rejection; allergy; antibody 26; heavy chain variable region; VH. 61 GKGLEWLGVIWAGGTINYNSALMSRLFISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120 1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60 0; Gaps Novel antibody-toxic group conjugate comprising an antibody that recognizes a molecule expressed only on activated T cells, useful for modulating immune response for treating autoimmune disorder, allergic Length 142; Indels 100.0%; Score 742; DB 22; 100.0%; Pred. No. 4.3e-60; tive 0; Mismatches 0; Mouse antibody 26 heavy chain variable region. AAG66520 standard; Protein; 142 AA. 121 AMMKRGYAMDYWGQGTLVTVSS 142 121 ammkrgyamdywgqgtlvtvss 142 Claim 15; Fig 10; 123pp; English. 27-JAN-2000; 2000US-0178473. 26-JAN-2001; 2001WO-US02653. (GEMY) SENETICS INST INC. 22-OCT-2001 (first entry) Conservative Similarity 142 AA; WO200154732-A1. Mus musculus. 02-AUG-2001.

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The invention relates to an antibody-toxic group conjugate comprising an antibody that specifically recognises a molecule expressed only on a ctivated T cells, and a toxic group. The T cell molecule is crivated T cells, and a toxic group. The T cell molecule is preferably human cytotoxic T lymphocyte associated antigen 4 (CTLA4). The antibody of the invention is a humanised anti-CTLA4 antibody comprising a sequence of 128 or 142 amino acids fully defined in the congrising a sequence of 128 or 142 amino acids fully defined in the appearance of 128 or 142 amino acids fully defined in the specification. The antibody-toxic group conjugate is useful for condition such as autoimmune disorder, immune response to a praft, or condition such as autoimmune disorder, immune response to a therapeutic protein.

The antibody is also useful for research purposes, e.g., in staining the antibody is also useful for research purposes, e.g., in staining the facility for isolating specific IL-2 receptor-bearing cells or T-cell typing, for isolating specific IL-2 receptor-bearing cells or T-cell typing, for isolating specific IL-2 receptor-bearing cells or T-cell typing, for isolating specific IL-2 receptor-bearing cells or the effectiveness of an agent to down-regulate CTLA4 activity. The thesent sequence is the heavy chain variable region of mouse continuody of the invention.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              HuM4TS.22; antibody; platelet derived growth beta receptor; PDGF-R beta; inhibition; intimal hyperplasia; vasculature; restenosis; angioplasty;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             0; Gaps
                                                                                                                  Novel antibody-toxic group conjugate comprising an antibody that recognizes a molecule expressed only on activated T cells, useful for modulating immune response for treating autoimmune disorder, allergic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /note= "Complementarity determining region 1"
Turner K, Collins M, Gray GS, Morris D;
Tsurushita N;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Score 664; DB 22; Length 142; Pred. No. 5.1e-53;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            6; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                8; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                /note= "Mature Protein"
49..54
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               AAW30273 standard; Protein; 137 AA.
                                                                                                                                                                                                                    Example 7; Page 84; 123pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       121 ammkrgyamdywgqgtsvivss 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                89.5%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          07-JUL-1998 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Heavy chain of HuM4TS.22.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Best Local Similarity 88.09
Matches 125; Conservative
                       f, Wood C,
Hinton P,
                                                                              2001-483195/52.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Sequence 142 AA;
                                                                                                  N-PSDB; AAH76438
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Homo sapiens.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           AAW30273;
                             Carreno BM,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Protein
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Query Match
                                               O'Hara D,
                                                                                                                                                                                               response
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAW30273
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Antibodies to platelet derived growth factor beta receptor - inhibit PDGF BB-induced proliferation of cells expressing the receptor, used particularly for inhibiting intimal hyperplasia
                                                                                                                                                                                                                                          (BOEF ) BOEHRINGER MANNHEIM GMBH.
                                                                                                                                                                                                                                                 (PROT-) PROTEIN DESIGN LABS INC.
                                                                                                                                                                                                                                                                                                                     Claim 6; Fig 2C; 87pp; English.
                                                                                                                                                                                                                                                             Chang CN, Landolfi NF,
                                                                                                                                                            Misc-difference 102
                                                             Misc-difference 56
                                                                                                                                                                                                                                                                         WPI; 1997-503114/46.
                                           Misc-difference 49
                                                                                Misc-difference 66
                                                                                                   Misc-difference 86
                                                                                                                      Misc-difference 92
                                                                                                                                         Misc-difference 93
                        Misc-difference
                                                                                                                                                                                                                                                                                N-PSDB; AAT90980
Binding-site
             Binding-site
                                                                                                                                                                                      WO9737029-A1
                                                                                                                                                                                                                 19-MAR-1997;
                                                                                                                                                                                                                             22-MAR-1996;
                                                                                                                                                                                                    09-OCT-1997.
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This is the amino acid sequence for the heavy chain of HuM4TS.22, a novel antibody which specifically binds to the platelet derived growth beta receptor (PDGF-R beta), but not within the fifth extracellular Ig-like domain, where the antibody inhibits PDGF BB-induced proliferation of a cell expressing the PDGF beta receptor. The antibody can be used in a method of inhibiting intimal hyperplasis in the vasculature of a manmal. The antibodies can be used for the treatment of disorders related to PDGF activity such as disorders involving proliferation of smooth muscle cells, and including restenosis following angioplasty. 137 AA; Sequence

; Length 137; 14; Indels DB 18; 81.3%; Score 603.5; DB 1 83.1%; Pred. No. 1.5e-47; ive 5; Mismatches 14 Conservative Similarity Matches 118; Query Match Best Local

1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60

Dp δ

61 GKGLEWLGVIWAGGTINYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120 Antibody, light chain; variable region; hybridoma cell line 44H104; immune response; enhance; stimulate; vaccine; immunodiagnosis; Murine anti-human class II monoclonal antibody 44H104 VH chain. Klein MH; Caterini JE, Cates GC, AAW22538 standard; Protein; 140 AA. 121 AMMKRGYAMDYWGQGTLVTVSS 142 117 -tgtrgyffdywgggtlvtvss 137 96WO-CA00400. 95US-0483576. (first entry) (CONN-) CONNAUGHT LAB LTD. Barber BH, WPI; 1997-077271/07. antigen delivery. N-PSDB; AAT77852. Mus musculus. WO9640941-A1. 03-NOV-1997 07-JUN-1996; 07-JUN-1995; 19-DEC-1996. AAW22538; Anand NN, Dp δ δ

/note= "Optionally Ser at position 37 of the mature

protein

/note= "Optionally Ser at position 30 of the mature

protein"

/note= "Optionally Asn at position 1 of mature protein" /note= "Complementarity determining region 3" "Complementarity determining region 2"

116..126 68..84 /note/note= "Optionally Ile at position 48 of the mature

protein

/note= "Optionally Ile at position 67 of the mature

/note= "Optionally Val at position 73 of the mature

/note= "Optionally Leu, Ile, and Met at position 74 /note= "Optionally Ile at position 74 of the mature

of the mature protein"

protein"102

Martin U;

96US-0621751. 97WO-US04198.

Recombinant conjugate antibody mol., modified for delivering an antigen - elicits enhanced immune response without the use of adjuvant to generate antibodies which are useful in vaccines or immuno:diagnosis

Example 1; Fig 1B; 64pp; English.

Novel recombinant conjugate antibody molecules comprise a monoclonal antibody specific for a surface structure of antigen presenting exclusively at one or more preselected sites. The conjugate is capable of delivering the antigen to APC and eliciting an immune response to the antigen. The new conjugates are useful as vaccines and are able to elicit an enhanced immune response without the use of an adjuvant. In a specific example, a conjugate was constructed using the murine anti-human class II monoclonal antibody secreted by hybridoma at andemly linked T and B cell epitope derived from HIV MN strain. The present sequence represents the heavy chain variable region anti-na trunch and a capable of the preparation of a conjugate with

Sequence 140 AA;

4; Gaps 73.5%; Score 545; DB 18; Length 140; 76.2%; Pred. No. 3.1e-42; ive 12; Mismatches 18; Indels 73.5%, 76.2%; Prev. Conservative Similarity Best Local Sim Matches 109; Query Match

1 MAVLVLFLCLVAFPSC-VLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQP 59 οy pp

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AAR98941 standard; Protein; 151 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                       (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                     WPI; 1996-277724/28.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            151 AA;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 N-PSDB; AAT34815
                                                                                                                                                                                                                                                                                                                                                                                             02-DEC-1994;
                                                                                                                                                                                                                                                                                                                                                                    28-NOV-1995;
                                                                                                                                                                            musculus.
                                                                                                                                                                                                                                                                                                                    WO9616990-A1
                                                                                                                                                                                         Homo sapiens
                                                                                                                                                                                                                                                                                                                                            06-JUN-1996
                                                                       03-JAN-1997
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sednence
                                                                                                                                                                                                                                                                                                                                                                                                                                              Ellis JH,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Query Match
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                                                AAR98941;
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9
             AAR98941
RESULT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            7
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The present invention describes an antibody, which can react specifically with ganglioside GD2, and is transplanted with a human type complementation-determining domain (CDR), or its fragments. The antibody and its derivatives are useful in diagnosis and therapy of tumours, particularly cancer diagnosis. The present sequence is a protein used in the exemplification of the invention.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Human type complementation-determining domain transplanted antibody and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               derivatives against ganglioside GD2, useful in diagnosis and therapy of e.g. tumours, has low antigenicity, little side effects but potent
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNOVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1 MAVIVLFLCIVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Gaps
                 60 PGKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPP 119
                                                                                                                                                                                                                                              Ganglioside; GD2; complementation determining region; CDR; antibody;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     DB 22; Length 137;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     73.0%; Score 541.5; DB 22; Length llarity 74.1%; Pred. No. 6.3e-42; Conservative 15; Mismatches 15; Indels
                                                                                                                                                                                                                       Ganglioside GD2 specific antibody related protein #1.
                                                                                                                                                                                                                                                                                                                                                                                                                                            Niwa R;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Example 2; Page 96-97; 123pp; Japanese.
                                                                                                                                                                                                                                                                                                                                                                                                                                              Nakamura K,
                                                                                                                                                  AAB81975 standard; Protein; 137 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                121 AMMKRGYA-MDYWGQGTLVTVSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     117 --rsddyswfaywgggtlytysa 137
                                                                                    121 dyv---hyamdywgqgtsvtass 140
                                                          120 HAMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                    (KYOW ) KYOWA HAKKO KOGYO KK
                                                                                                                                                                                                                                                                                                                                                                  29-SEP-2000; 2000WO-JP06773.
                                                                                                                                                                                                                                                                                                                                                                                           99JP-0278290.
                                                                                                                                                                                                    (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                               Shitara K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                     WPI; 2001-266163/27.
N-PSDB; AAF86854.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Best Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  activity in cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       137 AA;
                                                                                                                                                                                                                                                                                                                    WO200123573-A1.
                                                                                                                                                                                                                                                                    mouse; cancer.
                                                                                                                                                                                                                                                                                                                                                                                              30-SEP-1999;
                                                                                                                                                                                                                                                                                             Mus musculus.
                                                                                                                                                                                                      03-JUL-2001
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Matches 106;
                                                                                                                                                                                                                                                                                                                                            05-APR-2001
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                                                Hanai N,
                                                                                                                                                                            AAB81975;
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61 GKGLEWLGVIWAGGTINYNSALMSRLTISKDISKNOVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                A monoclonal antibody (MAb) which has donor CDR's of foreign origin and a recipient framework of human or primate origin, where the original amino acid at position 29 or 78 of the heavy (H) chain of the framework is replaced by an amino acid the same as or similar to that in the corresponding position of the H chain of the Ab from which the CDR's are derived, can be used for the treatment of cancer, and autoimmune diseases, specifically multiple myeloma, lymphoma and residues 29 and 78 of the humanised Ab with the original donor residues restores the antigen binding activity of the antibodies.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Humanised monoclonal antibodies with donor framework residues 29 an 78 - esp. against CD38, useful for treating cancer and auto-immune
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               4
                                                     Monoclonal antibody; MAb; humanised; cancer; autoimmune disease; multiple myeloma; lymphoma; rheumatoid arthritis; CD38; complementary determining region; CDR; heavy chain; light chain.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              71.4%; Score 530; DB 17; Length 151; 69.7%; Pred. No. 7.8e-41;
Humanised anti-CD38 monoclonal antibody variable heavy chain.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  19; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Disclosure; Figure 1; 92pp; English.
                                                                                                                                                                                                                                                              Location/Qualifiers
                                                                                                                                                                                                                                                                                            52..56
/label= CDR 1.
71..86
                                                                                                                                                                                                                                                                                                                                                                        /label= CDR 2.
119..129
                                                                                                                                                                                                                                                                                                                                                                                                                                 /label= CDR 3.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      94GB-0024449.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                95WO-GB02777
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (WELL ) WELLCOME FOUND LID.
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Matches 99; Conservative
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monoclonal antibodies (MADs) eg CDRs from mouse MAD can be partially or totally grafted into the framework regions of a human MAD, which is then produced in quantity by a suitable cell line. CDS= complementarity determining regions. The antilysozyme antibody two Kappa light chains (K).
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          The method of the invention is used for "humanising" non-human
                                                                                                                                                    Recombinant altered antibody; humanised monoclonal antibody.
                                                                                                                      Sequence of the heavy chain variable region of the Dl.3
                                                                                                                                                                                                                    /note= "residues which contact lysozyme"
                                                                                                                                                                                                                                         "residues which contact lysozyme"
                                                                                                                                                                                                                                                              "residues which contact lysozyme"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Recombinant altered antibodies - having complementarity determining regions replaced with those from antibody of different specificity
                                                        AAP70991 standard; Protein; 135 AA.
                                                                                                                                                                             Location/Qualifiers
      119 smittgfvmdswgggtsvtvss 140
                                                                                                                                                                                                  /label= Signal
                                                                                                                                                                                                                                                                                 /label= CDR 1
                                                                                                                                                                                                                                                                                                        /label- CDR 2
                                                                                                                                                                                                                                                                                                                     117..124
/label= CDR 3
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Example; Fig 7; 41pp; English.
87EP-0302620.
                                                                                                                                                                                                                                                                                                                                                                                                                      87GB-0007252.
                                                                                                    (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                              86GB-0007679
                                                                                                                                                                                                                                                                                                                    24
                                                                                                                                                                                                                                                      .121
                                                                                                                                                                                                                                            /note=
118..12
                                                                                                                                                                                                                                                                /note=
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 WPI; 1987-272811/39.
                                                                                                                                                                                                                                                                                                                                                                                                                                          (WINT/) WINTER G P.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                135 AA;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          N-PSDB; AAN72111.
                                                                                                   20-JUN-1991
                                                                                                                                                                                                                                                                                                                                                                                      26-MAR-1987;
                                                                                                                                                                                                                                                                                                                                                                                                         27-MAR-1986;
                                                                                                                                                                                                                                                                                                                                                                                                                      26-MAR-1987;
                                                                                                                                                                                                                                                                                                                                                                  30-SEP-1987
                                                                                                                                                                                                                                                                                                                                             EP239400-A.
                                                                              AAP70991;
                                                                                                                                                                                                                                                                                                                                                                                                                                                             Winter GP;
                                                                                                                                                                                     Peptide
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence
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                                                AAP70991
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MuM4TS.22; antibody; platelet; beta receptor; PDGF-R beta; inhibition; intimal hyperplasia; vasculature; restenosis; angioplasty; heavy chain.
61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVȚAADTAVYYCARGPPH 120
                                 This is the amino acid sequence for the heavy chain of muM4TS.22, a novel antibody which specifically binds to the platelet derived growth beta receptor (PDGF-R beta), but not within the fifth extracellular Ig-like domain, where the antibody inhibits PDGF The antibody can be used in a method of inhibiting intimal hyperplasia in the vasculature of a mammal. The antibodies can be used for the intenament of disorders related to PDGF activity such as disorders involving proliferation of smooth muscle cells, and including
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Antibodies to platelet derived growth factor beta receptor - inhibit PDGF BB-induced proliferation of cells expressing the receptor, used particularly for inhibiting intimal hyperplasia
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    "Complementarity determining region 1"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        "Complementarity determining region 2"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       /note= "Mature protein"
                                                                                                                                                                                                                                                                                                               AAW30277 standard; Protein; 137 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Martin U;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (BOEF ) BOEHRINGER MANNHEIM GMBH. (PROT-) PROTEIN DESIGN LABS INC.
                                                                                                                 121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                      117 ---erdyrldywgggttltvss 135
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     restenosis following angioplasty.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Claim 4; Fig 1D; 87pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                96US-0621751.
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                                                                                                                                                                                                                                                                                                                                                                                                                                 07-JUL-1998 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Heavy chain of MuM4TS.22.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Chang CN, Landolfi NF,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /note-
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             N-PSDB; AAT90984
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                                                                                                                                                                                                                                                                                                                                                                          AAW30277;
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Score 527.5; DB 18; Length 137; Pred. No. 1.2e-40;

71.1%; 71.1%;

Best_Local Similarity

Query Match

7; Gaps

20; Indels

DB 8; Length 135;

71.4%; Score 529.5; DB 8 71.1%; Pred. No. 7.6e-41; ive 14; Mismatches 20

Best Local Similarity (1.13) Matches 101; Conservative

Query Match

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AAW01146;

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61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                   4; Gaps
                                                                                                                                                  1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                                                                                                                   Antibody engineering; humanised antibody; chimeric antibody; Fab; interleukin-5; IL-5; eosinophil; asthma; allergic rhinitis; atopic dermatitis; therapy; diagnosis; heavy chain; VH;
                                                                              71.0%; Score 527; DB 17; Length 138; 71.1%; Pred. No. 1.3e-40; tive 14; Mismatches 23; Indels '
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Cook RM, Gross MS;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   NEWM humanised 2B6 antibody heavy chain variable region.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /_oct= "mouse MAD 2B6 VH CDR3"
109.119
/note= "human NEWM framework region"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /note= "human NEWM framework region"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   "human NEWM framework region"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              "mouse MAb 2B6 VH CDR2"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /note= "mouse MAb 2B6 VH CDR1"
particularly suitable for preclinical testing.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Chaiken IM,
Theisen TW;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                       AAR98492 standard; Protein; 119 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               (SMIK ) SMITHKLINE BEECHAM CORP. (SMIK ) SMITHKLINE BEECHAM PLC.
                                                                                                                                                                                                                                                                                                 121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                                                                                                                                                  121 gf----yamdywgqgtsvtvss 138
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94US-0363131.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /label= CDR3
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          95WO-US17082.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /label= CDR1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           12-OCT-1996 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Appelbaum ER,
, McMillan LJ,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              monoclonal antibody; MAb.
                                                                                                                          Matches 101; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       08
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                                                                                         Query Match
Best Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                22-DEC-1995;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 23-DEC-1994;
06-JUN-1995;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Synthetic.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                             AAR98492;
                                            Sequence
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Region
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           SXX
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 wonoclonal antibodies which inhibit type II phospholipase A2 are useful in the treatment of myocardial infarction, cerebral useful in the treatment of myocardial infarction, cerebral paraction, acute kidney failure, chronic rheumatism, cardiac shock, infarction, acute kidney failure, chronic rheumatism, cardiac shock, pancreatitis, adult respiratory distress syndrome and colitis. The antibodies were generated by immunishing Balb/C mice with recombinant human type II phospholipase A2. Spleen cells from the mice were cised with mouse myeloma P301 (P3x63Ag8.U1) and the hybridomas obtained were screened for phospholipase A2 inhibitory activity.

Active clones were isolated including 12H5, 1.4 and 10.1. These cultured and the antibody 12H5, 1.4 and 10.1. These supernatant by precipitation with ammonium sulphate and purification supernated for protein A:Sepharose CLAB. Because the antibody acts on the primate and mouse forms of enzyme as well as human it is
                ij
                                                                                                                                     61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120
                  5; Gaps
                                               1 MAVLVLFLCLVAFPSCVLSGVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                  Monoclonal antibody; phospholipase; myocardial infarction; pancreatitis; cerebral infarction; acute kidney failure; colitis; chronic rheumatism; adult respiratory distress syndrome; cardiac shock; treatment; preclinical testing; disease; hybridoma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Monoclonal antibody inhibiting type II phospholipase A2 activity for treatment of myocardial and cerebral infarction
                                                                                                                                                                                                                                                                                                                                                                                                               MAb 10.1 heavy chain, directed against type II phospholipase A2.
                14; Mismatches 22; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Yasunaga T;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Kawauchi Y, Masuho Y, Takasaki J,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Claim 6; Figure 14; 69pp; Japanese.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Location/Qualifiers
                                                                                                                                                                                                                                                                                                                  AAW01146 standard; Protein; 138 AA.
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                                                                                                                                                                                            121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                                   /label= CDR 2
117..127
/label= CDR 3
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/label= CDR 1
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                       Matches 101; Conservative
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Mus musculus.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Binding-site
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The heavy chain variable region (AAR98492) of NEWM humanised antibody 2B6 comprises complementarity determining regions (see also AAR98480-82) derived from murine monoclonal antibody 2B6 VH (see also AAR98478) and framework regions from human immunoglobulin NEW, but with antino acid substitutions made at framework residues that might influence CDR presentation. A synthetic variable light chain sequence (AAR98493) was also constructed. Humanised 2B6 (see also AAR98488-89) is specific for human interleukin-5 (IL-5) and can be used for the diagnosis and treatment of IL-5-mediated conditions, e.g. asthma, allergic rhinitis and atopic dermatitis.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Humanised immunoglobulin; mouse; human; antibody; heavy chain; diabetes; light chain; graft versus host disease; transplant; autoimmune disease; multiple sclerosis; rheumatoid arthritis; systemic lupus erythematosus; myasthenia gravis; herpes infection; myeloid leukaemia; CMV infection.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            80 SALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPHAMMKRGYAMDYWQQGTLVT 139
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                20 QVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPPGKGLEWLGVIWAGGTTNYN 79
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               New monoclonal antibody to human interleukin-5 - used to produce products for the treatment and diagnosis of conditions associated with excess eosinophil prodn., e.g asthma etc.
                                                                                                                                                                                                                                                                                                                                                                                                         tch 70.8%; Score 525; DB 17; Length 119; al Similarity 81.3%; Pred. No. 1.7e-40; 100; Conservative 11; Mismatches 8; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Murine mik-betal antibody heavy chain SEQ ID NO: 33.
                                                                                                                                 Claim 28; Page 87-88; 120pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    AAB69656 standard; Protein; 138 AA.
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                 1996-333976/33.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Queen CL, Selick HE;
                                                                                                                                                                                                                                                                                                                                                                                                                             Best Local Similarity
                                                                                                                                                                                                                                                                                                                                                            119 AA;
                                  N-PSDB; AAT34095
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 140 VSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 117 vss 119
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        30-APR-2001
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               US6180370-B1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                07-JUN-1995;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    13-FEB-1989;
28-SEP-1990;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 30-JAN-2001.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  28-DEC-1988;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    19-DEC-1990;
                                                                                                                                                                                                                                                                                                                                                            Sequence
                                                                                                                                                                                                                                                                                                                                                                                                               Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        AAB69656;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Mus sp.
                                                                                                                                                                                                                                                                                                                                                                                                                                             Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   RESULT 11
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The present invention describes a method of producing humanised immunoglobulins involving expressing in a cell a nucleic acid encoding a humanised version of an immunoglobulin. This is obtained by comparing a donor and human immunoglobulin and producing a combined antibody which graft-versus host disease, transplant rejection, autoimmune diseases such as diabetes, rheumatoid arthritis, myasthenia gravis, multiple sclerosis and systemic lupus erythematosus, herpes infections, CMV virus infections and myeloid leukaemia. The present sequence is an antibody used to demonstrate the method of the invention.
                                                                                                                                                                                                                                                                                                                                                                                                                                                  61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP 60
                                                                                                                                                                                                                                                                                                                                                                                                          4; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         interleukin'5; IL-5; human; eosinophil; asthma; allergic rhinitis; atopic dermatitis; therapy; diagnosis; humanised antibody.
                                         Producing humanized immunoglobulin, involves producing a cell containing DNA segments encoding humanized heavy and light chain variable regions, and expressing the DNA segments in the cell-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Neutralising antibody; monoclonal antibody; MAb; 2B6; NEW; mouse;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     "2B6 complementarity determining region 1"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       "2B6 complementarity determining region 2"
                                                                                                                                                                                                                                                                                                                                 70.8%; Score 525; DB 22; Length 138; 70.4%; Pred. No. 2e-40; tive 21; Mismatches 17; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            "NEW framework region 1"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                "NEW framework region 2"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    "NEW framework region 3"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                NEWM humanised heavy chain variable region.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Location/Qualifiers
                                                                                                 Example 5; Fig 23; 145pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAW42471 standard; Protein; 119 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           CDR2
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      /label= CDR1
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    36..49
/label= FR2
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        66..97
/label= FR3
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   22-JUN-1998 (first entry)
                                                                                                                                                                                                                                                                                                                                                                 Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Chimeric - Mus musculus.
Chimeric - Homo sapiens.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /label=
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            'note=
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       /note=
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WPI; 2001-190856/19.
                                                                                                                                                                                                                                                                                                                                                Similarity
                                                                                                                                                                                                                                                                                         138 AA;
               N-PSDB; AAF58728
                                                                                                                                                                                                                                                                                                                                                  Best Local Sim
Matches 100;
                                                                                                                                                                                                                                                                                         Sequence
                                                                                                                                                                                                                                                                                                                                   Query Match
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                                                                                                                                                                                                                                                                                                                                                                         4; Gaps
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1;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                   This polypeptide comprises a humanised antibody heavy chain variable region composed of human NEW framework regions and complementarity determining regions (see AAW4257.59) derived from anti-human interleukin-5 (hlL-5) murine monoclonal antibody (MAb) case haw42451). It is encoded by a DNA construct case AAW4251 hr vector powlibs NEW. The invention provides so intibodies, especially altered, chimeric and humanised antibodies antibodies, especially altered, chimeric and humanised antibodies and affinity for hIL-5. The antibodies are useful for treating chin-frinty for hIL-5. The antibodies are useful for treating chin-friendiated disorders such as asthma, allergic rhinitis and atopic dermatitis, and can also be used in the diagnosts of such conditions by measurement (e.g. by ELISA) of endogenous hIL-5 conditions by measurement (e.g. by ELISA) of endogenous hIL-5 expression of the novel antibodies.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             80 SALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPHAMMKRGYAMDYWGQGTLVT 139
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        4; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     20 QVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPPGKGLEWLGVIWAGGTTNYN 79
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Use of neutralising antibody to human interleukin-5 - that does not block binding to receptor alpha chain, to treat e.g. asthma, allergic rhinitis or atopic dermatitis
              /label= CDR3
/note= "2B6 complementarity determining region 3"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Length 119;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      70.4%; Score 522; DB 19;
80.5%; Pred. No. 3.2e-40;
                                                                               /note= "NEW framework region 4"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Heavy chain variable region of M225 antibody.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        est_Local Similarity 80.5%; Pred. No. 3.2e
ptches 99; Conservative 12; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 AAW08942 standard; Protein; 138 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                Example 4; Fig 12; 116pp; English.
                                                                                                                                                                                                                                                        (SMIK ) SMITHKLINE BEECHAM CORP.
                                                                                                                                                                                     97WO-US10769.
                                              109..119
/label- FR4
                                                                                                                                                                                                                      96US-0667769
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                                                                                                                                                                                                                                                                                        Cook RM;
98..108
                                                                                                                                                                                                                                                                                                                           WPI; 1998-062853/06.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 119 AA;
                                                                                                                                                                                                                                                                                                                                             N-PSDB; AAV03505.
                                                                                                                                                                                                                                                                                          Appelbaum ER,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               140 VSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              117 vss 119
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                                                                                                                      WO9748418-A1
                                                                                                                                                                                     20-JUN-1997;
                                                                                                                                                                                                                        21-JUN-1996;
                                                                                                                                                       24-DEC-1997
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     AAW08942;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Query Match
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   Region
                                                  Region
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61 GKGLEWLGVIWAGGTTNYNSALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPH 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            The present sequence is the heavy chain variable region of the murine monoclonal antibody (MAb) M225, which is specific for the human epidermal growth factor (EGF) receptor. The MAb, or a fragment, can be used to inhibit the growth of tumour cells, especially late stage prostatic tumour cells in humans, optionally conjugated to a cytotoxic agent, especially doxorubicin, taxol or cisplatin, or a signal transduction, ras or cell cycle
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1 MAVLVLFLCLVAFPSCVLSQVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPP
Heavy chain; murine; mouse; monoclonal; antibody; M225; human; epidermal growth factor; EGF; receptor; inhibition; growth; tumour; cell; late stage; prostatic; prostate; variable region.
                                                                                                                                                                                                                                                                                                                       Chimeric and humanised versions of anti-EGF receptor antibody 225 used for inhibiting tumour growth, esp. of late stage prostatic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     4;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Length 138;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                B-cell lymphoma; humanised antibody; bispecific antibody; myeloma; leukaemia; hybridoma; monoclonal antibody.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   21; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Humanised 1D10 antibody heavy chain variable region.
                                                                                                                                                                                                                                                     Saldanha JW;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        69.8%; Score 518; DB 18;
68.3%; Pred. No. 8.6e-40;
iive 20; Mismatches 21;
                                                                                                                                                                                                                                                      Giorgio NA, Goldstein NI, Jones ST,
                                                                                                                                                                                                                                                                                                                                                                                Example IV; Fig 14; 112pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AAW05823 standard; Protein; 116 AA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          121 AMMKRGYAMDYWGQGTLVTVSS 142
                                                                                                                                                                                                             (IMCL-) IMCLONE SYSTEMS INC. (MRCC-) MRC COLLABORATIVE CENT.
                                                                                                                                                                       95US-0573289.
95US-0482982.
                                                                                                                                            96WO-US09847.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        97; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Chimeric Homo sapiens;
Chimeric Mus sp.
                                                                                                                                                                                                                                                                                    WPI; 1997-051897/05.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      138 AA;
                                                                                                                                                                                                                                                                                                  N-PSDB; AAT49340
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  27-JAN-1997
                                                                                                                                                                      15-DEC-1995;
07-JUN-1995;
                                                                                       WO9640210-A1
                                                                                                                                             07-JUN-1996;
                                                                                                                   19-DEC-1996.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Sequence
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Query Match
                                                              Mus spp.
                                                                                                                                                                                                                                                                                                                                                          tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 RESULT 14
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Location/Qualifiers

31..35 /label≈ CDR1 /label= CDR2 98..105 /label= CDR3 /note= "human framework residue 27 is substd. by

equivalent murine framework residue"

/note= "human framework residue 29 is substd. by

equivalent murine framework residue"

/note= "human framework residue 30 is substd. by

equivalent murine framework residue"

/note= "human framework residue 37 is substd. by

equivalent murine framework residue"

/note= "human framework residue 68 is substd. by

equivalent murine framework residue"

/note= "human framewoek residue 73 is substd. by

equivalent murine framework residue"

equivalent murine framework residue"

equivalent murine framework residue"

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Misc-difference 82
/note= "human framework residue 82 is substd. by a consensus amino acid of the equivalent murine framework residue"
                                                                                        Misc-difference 71
/note= "human framework residue 71 is substd. by
                                                                                                               Misc-difference 29
                                                                 Misc-difference 37
                                                      Misc-difference 30
                                                                             Misc-difference 67
                                                                                                    Misc-difference 73
                              Misc-difference
                                                                                                                                               WO9626964-A1
        Region
                Region
                       Region
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The variable region (AAW05823) of the humanised 1D10 antibody heavy chain (AAW05829) consists of human 1C4 heavy chain variable region framework (substd. at 9 positions with mouse or consensus human murine 1D10 antibody specific for a 28/32 kDa heterodimeric antigen present on the surface of malignant B-cells. It can be coexpressed myeloma NSO cells. Humanised along light chain (see also AAW05828) in e.g. mouse into novel bispecific antibodies reactive with both effector cell antigens (see also AAW05828) and malignant.
                                                                                                                                                                                                                                                                                                                                                                                                   New bispecific antibody reactive with both T or NK cells and malignant B cells - also their humanised forms and hybridomas producing them, useful for treating or preventing leukaemia,
                                                                                                                                                                                                                                                                                               Weiner G;
                                                                                                                                                                                    (IOWA-) IOWA IMMUNOTHERAPY INVESTIGATORS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Claim 14; Fig 4b; 85pp; English.
                                                                                                                                                                                                                     (PROT-) PROTEIN DESIGN LABS INC
                                                                                                                                                                                                                                                                              Gingrich R, Link BK, Tso JY,
                                                               96WO-US02754.
                                                                                                                           95US-0397411.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Lymphoma and myeloma
                                                                                                                                                                                                                                                                                                                                          WPI; 1996-412742/41.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      116 AA;
                                                            29-FEB-1996;
                                                                                                                           01-MAR-1995;
06-SEP-1996
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Claim 28; Fig 4d; 85pp; English.

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80 SALMSRLTISKDTSKNQVSLKLSSVTAADTAVYYCARGPPHAMMKRGYAMDYWGQGTLVT 139
                         Gaps
                                     20 QVQLQESGPGLVKPSQTLSLTCTVSGFSLTSYGVYWVRQPPGKGLEWLGVIWAGGTTNYN 79
                                                 69.5%; Score 515.5; DB 17; Length 116; 80.5%; Pred. No. 1.2e-39; 1.10e 10; Mismatches 7; Indels 7;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           New bispecific antibody reactive with both T or NK cells and malignant B cells - also their humanised forms and hybridomas producing them, useful for treating or preventing leukaemia,
                                                                                                                                                                                                                                                            B-cell lymphoma; humanised antibody; bispecific antibody; myeloma; leukaemia; hybridoma; monoclonal antibody.
                                                                                                                                                                                                                                                                                                                                                                                                                                                   /label= Fos_leucine_zipper 340..446
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          (IOWA-) IOWA IMMUNOTHERAPY INVESTIGATORS. (PROT-) PROTEIN DESIGN LABS INC.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Tso JY, Weiner G;
                                                                                                                                                                                                                                                                                                                                  1..116
/label= Variable_domain
                                                                                                                                                                                                                                           Humanised 1D10 antibody heavy chain.
                                                                                                                                                                                  AAW05827 standard; Protein; 273 AA.
                                                                                                                                                                                                                                                                                                                        Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                       50..65
/label= CDR2
98..105
                                                                                                                                                                                                                                                                                                                                                                                           /label= CDR3
                                                                                                                                                                                                                                                                                                                                                                                                                                       /label= Hinge
                                                                                                                                                                                                                                                                                                                                                     31..35
/label= CDR1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      96WO-US02754.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         95US-0397411.
                                                                                                                                                                                                                                                                                                                                                                                                                      /label= CH1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /label= CH3
                                                                                                                                                                                                                       27-JAN-1997 (first entry)
                   99; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                .273
                                                                                                                                                                                                                                                                                                                                                                                                                                . 234
                                                                                                                                                                                                                                                                                          Chimeric Homo sapiens;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Link BK,
Query Match
Best Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          lymphoma and myeloma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         WPI; 1996-412742/41.
                                                                                                                                                                                                                                                                                                     Chimeric Mus sp.
                                                                                                                 140 VSS 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              WO9626964-A1.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     29-FEB-1996;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       01-MAR-1995;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Gingrich R,
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